Opioid

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EFFECT OF CHRONIC COCAINE TREATMENT ON MU AND DELTA OPIOID RECEPTOR MESSENGER RNA LEVELS IN DIFFERENT BRAIN REGIONS. A.V. Azaryan, L.J. Grimm, B.J. Clock, B.M. Cox. Department of Pharmacology, Uniformed Services University of Health Sciences, Bethesda, MD.

We have investigated the possibility that chronic cocaine treatment alters the levels of mRNA for mu and delta opioid receptors in brain regions rich in dopaminergic innervation. Male Sprague-Dawley rats were treated with saline or cocaine (50 mg/kg/day) for 3 days, delivered by osmotic minipump. Expression of mu and delta opioid receptor mRNA in olfactory bulb, nucleus accumbens and caudate putamen (caudal and rostral parts) was estimated using quantitative competitive polymerase chain reaction (PCR) assays following reverse transcription. No changes in the levels of mRNA for delta opioid receptor were detected after exposure to cocaine in any of the brain regions examined. A significant increase in the level of mu receptor mRNA was detected in nucleus accumbens after 3 days cocaine treatment. In caudate-putamen and olfactory bulb no change in mu receptor mRNA was observed. In situ hybridization analysis also indicated elevated levels of mu receptor mRNA in nucleus accumbens after cocaine treatment for 3 days, with little change in other brain regions.

These results indicate that chronic cocaine administration can lead to the upregulation of mu opioid receptor mRNA in nucleus accumbens, the brain region specifically associated with the reinforcing properties of addictive drugs. We suggest that endogenous opioid systems in nucleus accumbens are regulated by dopaminergic mechanisms, and therefore are influenced by cocaine treatment. Opioid mechanisms may contribute to the behavioral actions of cocaine.

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b-ENDORPHIN RECEPTORS AT THE NEUROMUSCULAR JUNCTION IN THE MOUSE. A.A.L. Evans, M.E. Smith. Department of Physiology, University of Birmingham, Birmingham, B15-2TT.

The opioid peptide β-endorphin has been shown to increase the contractile strength of skeletal muscle upon stimulation via the motor nerve (Khan & Smith, 1995). Furthermore receptors for this peptide have been demonstrated on the membranes of skeletal muscle fibres (Hughes & Smith, 1990). The receptors have been shown to be of the δ-opioid subtype (Evans et al., 1995). In the present study we investigated the distribution of the receptors on the muscle membranes in normal and obese-diabetic mice.

Mice of approximately 12 weeks of age were killed by cervical dislocation, and the EDL and soleus muscles were removed. Twenty μm cryostat sections were prepared from the central regions of the muscles and specific binding sites for [^{125}I]β-endorphin were revealed using autoradiography. Adjacent sections were stained for acetylcholinesterase to reveal the endplate regions (Pestronk & Drachman, 1978). The distribution of the binding sites was compared to the distribution of the endplate regions using a light microscope linked to NIH image analysis software on an Apple Macintosh Computer.

In both the normal and the obese-diabetic mice 75-85% of endplate regions exhibited specific β-endorphin binding sites. In the normal mice the receptors were restricted to the endplate regions in most muscle fibres but in a few fibres they were present along their entire length. However, in the obese-diabetic mice the receptors were densely distributed along the entire length in over 70% of the muscle fibres. The restriction of the opioid receptors to the muscle endplate regions in the normal mice indicates that they are primarily involved with functions at the neuromuscular junction. It is possible that the increased incidence and altered distribution of δ opioid receptors on the skeletal muscle fibres in the obese-diabetic mice is associated with the presence of peripheral motor nerve defects.

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